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| EXAMINER | |
|---|---|
| LANDAU, SHARMILA GOLLAMUDI | |
| **ART UNIT** | **PAPER NUMBER** |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/847,945 | DESAI ET AL. | |
| | Examiner | Art Unit | |
| | Sharmila Gollamudi Landau | 1616 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *07 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,3-15,17,31-55 and 57-90* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-15, 17, 31-55, 57-90* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Receipt of Amendments/Remarks and Information Disclosure Statements filed 9/7/07 is acknowledged. Claims **1, 3-15, 17, 31-55, 57-90** are pending in this application.

### *Information Disclosure Statement*

The IDS of 9/7/07 has not been considered since Office Actions in copending applications are non-published documents. The examiner suggests citing the prior art cited in the copending applications in a PTO-1449.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

**Claims 1, 3-15, 17, 31-55, 57-90 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

The instant independent claims have been amended to recite, "wherein the effective amount of the composition is delivered in less than about 30 minutes", which is vague and indefinite. It is unclear if the intended limitation is directed to administering the composition is less than 30 minutes or if the intended limitation is directed to providing the entire dosage amount in less than 30 minutes, i.e. excluding sustained release of over 30 minutes. It is noted that the latter interpretation does not have support in the specification and thus prior art is applied according to the first interpretation.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

**Claims 1, 3-15, 17, 31-33, 38-41, 46-49, 54-55, 57-90 are rejected under 35 U.S.C. 103(a) as being unpatentable over Desai et al (5,439, 686) in view of Kunz et al (5,733,925) in further view of Westesen et al (6,197,349).**

Desai et al teach an anticancer (antineoplastic) drug, specifically taxol derivatives such as paclitaxel, is suspended in a protein walled shell. See abstract. The shell is not greater than about 10 microns, preferably less than 5 microns, and most preferably less than 1 micron (1000 nanometers). See column 5, lines 30-40. For intravenous administration, the particles may have a diameter size from 0.1-5 microns. See column 9, lines 15-16. Desai teaches the method of delivery for the instant particles allows the administration of substantially water insoluble pharmacologically active agents employing a much smaller volume of liquid and requiring greatly reduced administration time relative to administration volumes and times required by

prior art delivery systems (e.g., intravenous infusion of approximately one to two liters of fluid over a 24 hour period are required to deliver a typical human dose of 200-400 mg of taxol). See column 3, line 60 to column 4, line 5.

The particles may be formed using biocompatiable polymers, proteins, or polysaccharides. A preferred protein for the shell is albumin. See column 6, lines 40-45 and example 4. Taxol exhibits a unique mode of action on microtubule proteins responsible for the formation of the mitotic spindle. See column 1, lines 20-30. Desai teaches administration of the microparticulates are advantageous in targeting specific sites in the body; allows for the administration of water-insoluble actives; reduces administration time. See column 3, lines 60-67 to column 4, lines 1-5. The particles also are stable and low in toxicity. See examples 5 and 7. Example 8 teaches injecting the particles in a ten-minute period.

Desai does not teach the instant methodology of treating non-cancerous cell proliferation in blood vessels. Further, Desai does not teach an amorphous drug.

Kunz et al teach methods for inhibiting stenosis following vascular trauma or disease, cancer, diseases resulting from hyperactivity or hyperplasia of somatic cells. Example 7 discloses smooth muscle proliferation in the neointima. Kunz teaches direct or targeted delivery of therapeutic agents to vascular smooth muscle cells. See column 1, lines 15-35. Inhibiting stenosis following angioplasty is contemplated. See column 3, lines 54-62. The dosage forms are preferably in biodegradable microparticulates or nanoparticulates wherein the particles are formed of a polymer-containing matrix that biodegrades. Kunz et al teach conjugating the drug with a binding protein to target the cells and reduce toxicity. Example 7 notes the toxicity of a free drug versus a conjugated drug. See column 14, lines 25-33. Kunz teaches protein-coated

particulates. See column 25, line 20 to column 26, line 40. Therapeutic agents such as taxol or analogs are preferred therapeutic agents that are designed to target the cell activity without killing the cell. Taxol is taken into the cell and stabilizes the cell from further dividing. See column 4, lines 40-45 and column 13, lines 24-27. Examples of dosages include .001 to 100 mg/kg per day. See column 28, line48. For prevention of restenosis following angioplasty or an intervention that contributes to the acute proliferation of smooth muscle cells, a single pre-loading dose is given prior to or at the time of intervention with smaller chronic doses given two or three weeks after intervention. For example, a single dose may be administered about 24 hours prior to intervention, while multiple preloading doses may be administered daily for several days prior to intervention. See column 29, lines 10-15. Delivery of the active agents may be intravenous, intra-arterial (stents), or local delivery. See column 30, lines 56-65 and examples for stent deployment. Kunz teaches single administration protocol. See column 36, lines 50-55. Example 6 teaches infusion using a balloon catheter. Administration to a carotid, femoral, and coronary artery is taught. See examples. Example 3 teaches administering the dose in less than three to five minutes. Also note example 5 and 14.

Westesen et al teach nanoparticles containing various poorly water-soluble drugs. See abstract. Westesen teaches the use of an amorphous form of the drug to provide for better solubility and bioavailability of poorly water-soluble drugs than utilizing a crystalline form. See column 5, lines 45-56. Generally amorphous forms of a substance exhibit a higher solubility and a faster dissolution than the crystals forms since they do not require lattice energy.

It would have been obvious for one of ordinary skill in the art at the time the invention was made to utilize Desai's protein coated drug (antineoplastic drug taxol) for the treatment of

proliferation of non-cancerous cells in blood vessels (restenosis). One would have been motivated to do so since Kunz teaches inhibiting stenosis following vascular trauma, diseases resulting from hyperactivity or hyperplasia of somatic cells using cytotoxic drugs such as taxol or analogs. Kunz teaches taxol or its analogs are preferred therapeutic agents that are designed to target the cell activity without killing the cell. Taxol is taken into the cell and stabilizes the cell from further dividing. to reduce atherosclerosis or restenosis since taxol promotes the formation of usually stable microtubules inhibiting the normal dynamic reorganization of the microtubule network required for mitosis and cell proliferation. Furthermore, Desai et al also recognize taxol's unique mode of action on microtubule proteins responsible for the formation of the mitotic spindle. Therefore, one would have expected success by utilizing Desai's taxol to treat abnormal proliferation in the blood vessels since Kunz teaches taxol is an effective drug that prevents or reduces cell proliferation in the blood vessels.

Further, it would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize an amorphous drug form. One would have been motivated to do so since Westesen teaches the use of an amorphous form for better solubility and bioavailability of poorly water-soluble drugs. Moreover, one would reasonably expect success by applying Westesen's teachings to Desai since both are directed to poorly water-insoluble drugs.

***Response to Arguments***

Applicant's arguments with respect to the claims have been considered but are moot in view of the new ground(s) of rejection. However, the examiner will address applicant's arguments pertaining to Desai since the examiner has retained this reference.

Applicant argues that Desai does not teach the instant methodology or the instant delivery time.

Applicant's arguments filed 9/7/07 have been fully considered but they are not persuasive. The examiner directs applicant's attention to example 8. Desai teaches administering the composition within ten minutes and thus Desai does not teach continuous infusion. In fact, Desai teaches the difference between the prior art, which teaches infusion over a 24-hour period and Desai's invention is the reduced administration time. The examiner notes that Desai does not teach the instant methodology and thus relies on Kunz. Kunz teaches taxol treats restenosis and Kunz teaches the instant delivery time.

Lastly, the applicant should note the 112, 2nd paragraph rejection. The examiner has made the rejection based on the first interpretation.

**Claims 34, 35, 42, 43, 50-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Desai et al (5,439, 686) in view of Kunz et al (5,733,925) in view of Westesen et al (6,197,349) in further view of Hunter (5,994,341).**

The teachings of Desai, Kunz, and Westesen have been discussed above. Desai teaches taxol exhibits a unique mode of action on microtubule proteins responsible for the formation of the mitotic spindle. See column 1, lines 20-30.

The references do not teach the specific use of epothilone as the antiproliferative agent.

Hunter teaches both epothilone and paclitaxel disrupt microtubule function. See column 15, lines 48-55.

It would have been obvious for one of ordinary skill in the art at the time the invention

was made to combine the teaching of the above references and utilize the instantly claimed drug. One would have been motivated to do so with a reasonable expectation of success since Hunter teaches that both paclitaxel and epothilone are both agents which disrupt microtubule function. The selection of a specific drug is considered prima facie obvious to a skilled artisan in the art.

**Claims 36-37, 44-45, 52-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Desai et al (5,439, 686) in view of Kunz et al (5,733,925) in view of Westesen et al (6,197,349) in further view of Gregory (Transplantation, vol. 59, pp. 655-661, 1995).**

The teachings of Desai, Kunz, and Westesen have been discussed above. Desai teaches the use of immunosupressants. See column 5, lines 60-63.

The references do not teach the specific use of rapamycin.

Gregory teaches rapamycin is an immunosuppressant which has an antiproliferative action, that is useful in the treatment of arterial thickening after injury such as angioplasty. See page 655.

It would have been obvious for one of ordinary skill in the art at the time the invention was made to combine the teaching of the above references and further use rapamycin to treat restenosis. One would have been motivated to do so with a reasonable expectation of success since Gregory teaches rapamycin is an immunosuppressant, which has an antiproliferative effect and thus is useful in treating restenosis. Therefore, a skilled artisan would have been motivated to further utilize rapamycin for its additive effect in treating restenosis.

**Claims 1, 3-15, 17, 31-33, 34-35, 38-41, 42-43, 46-49, 50-51, 54-55, 57-90 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hunter et al (5,716,981) by itself or in**

**view of Yapel (4,147,767) in further view of in view of Kunz et al (5,733,925) and Westesen et al (6,197,349).**

Hunter et al teach anti-angiogenic compositions comprising an anti-angiogenic factor and a polymeric carrier and methods of its use. See abstract and column 3, lines 40-45. Preferably the active compound is a compound that disrupts microtubule function such as paclitaxel, epothilone, and etc. see column 3, lines 60-65. The polymeric carrier may be chosen from a carbohydrate, protein, or polypeptide such as albumin, collagen, and gelatin. See column 18, lines 15-30. Hunter teaches using the composition to coat a stent which is inserted into the body. Delivery may be done through via expandable catheters. See column 4, lines 24-30 and column 22. Hunter teaches the use of the composition to treat non-tumorigenic angiogenesis dependent diseases. See column 5, lines 44-46 and column 36, lines 9-15. Specifically Hunter teaches methods of eliminating vascular obstructions in arteries and veins to prevent recurrent stenosis at the site of failed angioplasty and to treat post surgical narrowing. Suitable sites of the stent include iliac, renal, and femoral, and cornary arteries. See column 25, lines 48-67. Hunter teaches treating neointimal hyperplasia wherein a stent is coated with the composition and inserted onto the arteries. See column 36, lines 1-20. The composition may be further administered intarticularly, intravenously, etc. see column 37, line 67 to column 38, lines 1-10. The microspheres range from 50-nm to 500 microns depending on the particular use. See column 17, lines 25-40. Anti-angiogenic factors may be linked by occlusion in the matrices of the polymer, bound by covalent linkages, or encapsulated in microcapsules. See column 17, lines 1-5. Hunter teaches administering the anti-angiogenic composition using a stent. Example 7 teaches inserting the stent is into a rat. It should be noted that insertion of the stent would meet

the instant delivery time since the composition is delivered to the site in less than 30 minutes (the time it takes to insert a stent is less than 30 minutes).

The use of albumin as the polymeric carrier is not immediately envisaged and the examiner relies on Yapel to specifically provide motivation to use albumin. Further, although it appears that Hunter implicitly teaches the delivery time, Hunter does not specify the instant administration time and the examiner relies on Kunz for this teaching. Lastly, Hunter does not specify the drug form and the examiner relies on Westesen to teach this.

Yapel teaches albumin (HAS) medicament carrier suited for intravascular injections. Yapel teaches compared to prior art polymeric carriers has advantages such as ability to administer insoluble drugs; localizes the drug in the capillaries and the drug is released at the intended sire and reduces toxic side effects which is especially useful for anti-neoplastic drugs; the absence of emboli formation wherein albumin carriers are administered; ease of preparation; nonantigenicity; capability of carrying a variety of drugs. See column 2, line 50 to column 3, lines 30.

Westesen et al teach nanoparticles containing various poorly water-soluble drugs. See abstract. Westesen teaches the use of an amorphous form of the drug to provide for better solubility and bioavailability of poorly water-soluble drugs than utilizing a crystalline form. See column 5, lines 45-56. Generally amorphous forms of a substance exhibit a higher solubility and a faster dissolution than the crystals forms since they do not require lattice energy.

Kunz et al teach methods for inhibiting stenosis following vascular trauma or disease, cancer, diseases resulting from hyperactivity or hyperplasia of somatic cells. Example 7 discloses smooth muscle proliferation in the neointima. Kunz teaches direct or targeted delivery of

therapeutic agents to vascular smooth muscle cells. See column 1, lines 15-35. Inhibiting stenosis following angioplasty is contemplated. See column 3, lines 54-62. The dosage forms are preferably in biodegradable microparticulates or nanoparticulates wherein the particles are formed of a polymer-containing matrix that biodegrades. Kunz et al teach conjugating the drug with a binding protein to target the cells and reduce toxicity. Example 7 notes the toxicity of a free drug versus a conjugated drug. See column 14, lines 25-33. Kunz teaches protein-coated particulates. See column 25, line 20 to column 26, line 40. Therapeutic agents such as taxol or analogs are preferred therapeutic agents that are designed to target the cell activity without killing the cell. Taxol is taken into the cell and stabilizes the cell from further dividing. See column 4, lines 40-45 and column 13, lines 24-27. Examples of dosages include .001 to 100 mg/kg per day. See column 28, line48. For prevention of restenosis following angioplasty or an intervention that contributes to the acute proliferation of smooth muscle cells, a single pre-loading dose is given prior to or at the time of intervention with smaller chronic doses given two or three weeks after intervention. For example, a single dose may be administered about 24 hours prior to intervention, while multiple preloading doses may be administered daily for several days prior to intervention. See column 29, lines 10-15. Delivery of the active agents may be intravenous, intra-arterial (stents), or local delivery. See column 30, lines 56-65 and examples for stent deployment. Kunz teaches single administration protocol. See column 36, lines 50-55. Example 6 teaches infusion using a balloon catheter. Administration to a carotid, femoral, and coronary artery is taught. See examples. Example 3 teaches administering the dose in less than three to five minutes. Also note example 5 and 14.

Firstly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to look to the guidance provided by Hunter and utilize albumin as the polymer of choice. One would have been motivated to do so with a reasonable expectation of success and similar results since Hunter suggests proteins and polypeptides such as albumin are suitable as the polymeric carrier. Alternatively, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Hunter and Yapel and specifically utilize albumin as the polymeric carrier. One would have been motivated to do so since Yapel teaches the advantages of using albumin as the polymeric carrier including nonantigenicity, localized and targeted delivery which reduces toxicity of anti-neoplastic drugs, ease of preparation, etc.

Secondly, although it is the examiner's position that Hunter implicitly teaches the instant delivery time, i.e. by inserting a stent, it would have been obvious to administer the product in less than 30 minutes. One would have been motivated to do so since Kunz teaches administering microparticles and nanoparticles containing an antineoplastic drug via injections and stents in a single does regimen under 30 minutes. Further, Kunz teaches the dosing cycles to treat restenosis. A skilled artisan would have reasonably expected success and similar results since both Hunter and Kunz teach the treatment of recurrent stenosis and neointimal hyperplasia with drugs that inhibit microtubule function such as taxol. Therefore, it would have been obvious to look to Kunz to determine the appropriate delivery and dosing times to treat the same disease using the same delivery vehicle and drug.

Lastly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize an amorphous drug form. One would have been motivated to do so

since Westesen teaches the use of an amorphous form for better solubility and bioavailability of poorly water-soluble drugs.

***Response to Arguments***

Applicant's arguments with respect to the claims have been considered but are moot in view of the new ground(s) of rejection. However, the examiner will address applicant's arguments pertaining to Desai since the examiner has retained this reference.

Applicant argues that Hunter does not specify the instant dosing amount of delivery less than 30 minutes.

Applicant's arguments filed 9/7/07 have been fully considered but they are not persuasive. It is the examiner's position that Hunter implicitly teaches the delivery time. It is noted that Hunter teaches inserting a coated stent. Thus, although Hunter does not explicitly state that this is done under 30 minutes, the examiner points out that this is implicit since it takes less than 30 minute to place the catheter into a site. However, assuming arguendo that Hunter does not teach the amended limitation, the examiner relies on Kunz to cure this deficiency.

Lastly, the applicant should note the 112, 2nd paragraph rejection. The examiner has made the rejection based on the first interpretation.

**Claims 36-37, 44-45, 52-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hunter et al (5,716,981) by itself or in view of Yapel (4,147,767) in view of) Kunz et al (5,733,925) and Westesen et al (6,197,349) in further in view of Marx (Circ. Res. Vol. 76, pp. 412-417, 1995).**

The disclosure of Hunter, Yapel, Kunz, and Westesen have been set forth above.

The references do not teach the specific use of rapamycin as the antiproliferative agent.

Marx teaches rapamycin is an inhibitor of smooth muscle cells in the abnormal proliferation of restenosis. See abstract.

It would have been obvious for one of ordinary skill in the art at the time the invention was made to combine the teaching of the above references and utilize the instantly claimed drugs. One would have been motivated to do so with a reasonable expectation of success since Marx teaches the rapamycin is a smooth cell inhibitor useful in treating restenosis. The selection of a specific drug is considered prima facie obvious to a skilled artisan in the art.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

**Claims 1, 3-41, 46-49, 52-90 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3-17, 31-32, 38-40, 46-48, 54-90 over claims 1-2, 5-13, 16-17, 21 and 24 of copending Application No. 11/544242; instant claims 1, 3-17, 31-32, 38-40, 46-48, 54-90 over claims 1-2, 5-18**

**11/594417; and instant claims 1, 3-15, 17, 31-33, 36-41, 46-49, 52-53, 54-55, 57-90 over claims 1-49 of 11/359286 respectively in view of Kunz.**

The instant application is directed to a method of treating hyperplasia in the blood vessels and a method of reducing proliferation in vascular procedures comprising administering an antineoplastic; antiproliferative; or angiogenesis inhibitor coated with a protein.

Copending application '286 is directed to a method of treating a proliferative disease in an individual comprising administering to the individual: a) an effective amount of a composition comprising nanoparticles comprising a taxane and an albumin, and b) an effective amount of at least one other chemotherapeutic agent, wherein said chemotherapeutic agent is selected from the group consisting of antimetabolites, platinum-based agents, alkylating agents, tyrosine kinase inhibitors, anthracycline antibiotics, vinca alkloids, proteasome inhibitors, macrolides, and topoisomerase inhibitors. Dependent claims are directed to rapamycin, albumin, the instant route of administration; and particle size.

Copending application '242 is directed a method of treating a proliferative disease in an individual, comprising administering to the individual an effective amount of a composition comprising nanoparticles comprising a thiocolchicine (antineoplastic) or a derivative thereof and a carrier protein. Independent claim 13 is directed to treating a proliferative diseases comprising administering nanoparticles comprising orataxel and protein. Dependent claims are directed to albumin, the instant route of administration; and particle size.

Copending application '417 is directed to a method of treating a proliferative disease in an individual, comprising administering to the individual an effective amount of a composition

comprising nanoparticles comprising a taxane and a carrier protein. Dependent claims are directed to albumin, the instant route of administration; and particle size.

The copending applications do not specify the proliferative disease.

Kunz et al teach methods for inhibiting stenosis following vascular trauma or disease, cancer, diseases resulting from hyperactivity or hyperplasia of somatic cells. Example 7 discloses smooth muscle proliferation in the neointima. Kunz teaches direct or targeted delivery of therapeutic agents to vascular smooth muscle cells. See column 1, lines 15-35. Inhibiting stenosis following angioplasty is contemplated. See column 3, lines 54-62. The dosage forms are preferably in biodegradable microparticulates or nanoparticulates wherein the particles are formed of a polymer-containing matrix that biodegrades. Kunz et al teach conjugating the drug with a binding protein to target the cells and reduce toxicity. Example 7 notes the toxicity of a free drug versus a conjugated drug. See column 14, lines 25-33. Kunz teaches protein-coated particulates. See column 25, line 20 to column 26, line 40. Therapeutic agents such as taxol or analogs are preferred therapeutic agents that are designed to target the cell activity without killing the cell. Taxol is taken into the cell and stabilizes the cell from further dividing. See column 4, lines 40-45 and column 13, lines 24-27. Examples of dosages include .001 to 100 mg/kg per day. See column 28, line48. For prevention of restenosis following angioplasty or an intervention that contributes to the acute proliferation of smooth muscle cells, a single pre-loading dose is given prior to or at the time of intervention with smaller chronic doses given two or three weeks after intervention. For example, a single dose may be administered about 24 hours prior to intervention, while multiple preloading doses may be administered daily for several days prior to intervention. See column 29, lines 10-15. Delivery of the active agents may be

intravenous, intra-arterial (stents), or local delivery. See column 30, lines 56-65 and examples for stent deployment. Kunz teaches single administration protocol. See column 36, lines 50-55. Example 6 teaches infusion using a balloon catheter. Administration to a carotid, femoral, and coronary artery is taught. See examples. Example 3 teaches administering the dose in less than three to five minutes. Also note example 5 and 14.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the copending applications and Kunz to arrive at the instantly claimed invention of treating hyperplasia of blood vessels and deliver the composition in less than 30 minutes. One would have been motivated to do so since Kunz teaches neointimal hyperplasia is a proliferative disease that can be treated with anti-neoplastic drugs that disrupt microtubule function. Therefore, although the copending application do not specify treating hyperplasia, instant application and copending applications are directed to similar subject matter since hyperplasia is a proliferative disease.

This is a provisional obviousness-type double patenting rejection.

***Response to Arguments***

The examiner acknowledges applicant's statement that they will file a terminal disclaimer once allowable subject matter is identified.

***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila Gollamudi Landau whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

S. L. Landau

SHARMILA GOLLAMUDI LANDAU
PRIMARY EXAMINER

11/4/07

Sharmila Gollamudi Landau
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11/4/07